CHES STUDIES

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EVALUATION OF CANCER CLUSTER REPORTS IN NORTH CAROLINA

by

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ABSTRACT

North Carolinians have long been concerned about the patterns of cancer occurrence in the state, especially those that signal a potential environmental risk. Being increasingly faced with the task of responding to citizen reports of apparent cancer clusters (defined as the occurrence of an increased rate of cancer in a small area or within a short period of time), the North Carolina Department of Environment, Health, and Natural Resources implemented a formal program for the evaluation of the cluster reports in 1982. Mounting volume of cancer cluster reports and limited resources resulted in the development of a revised protocol involving the Cancer Surveillance Section of the Division of Statistics and Information Services and use of more databased evaluation procedures.

This report provides an overview of the current procedures in use for evaluating cancer cluster reports in North Carolina and highlights a few of the most interesting cluster evaluations over the last sixteen months. Since September 1989, forty-nine reports of cancer clusters have been received from thirty-one counties. Twenty-seven of these reports have been evaluated and closed. Eleven cluster reports are currently in the process of active evaluation and another eleven are awaiting the start of evaluation activities. Of the closed reports, five indicated increased cancer occurrence with three of the five potentially providing additional clues to environmental risk factors.

INTRODUCTION

A cancer cluster is the occurrence of a greater than expected number of cases of cancer within a small geographic area and/or within a short period of time (i.e., 3-5 years). Cancer clusters are usually reported when people learn that several friends, family members, neighbors or co-workers have been diagnosed with cancer. Because cancer is such a common disease, it is important to discover whether the cancers that have been observed truly represent the occurrence of more cases than one would expect.

The evaluation of cancer cluster reports may help to determine specific causes of cancer or to identify risks for cancer in the environment (Caldwell, 1989). Cancer cluster reports also serve an important social service as well by assuaging public anxiety over potential environmental cancer risks in their community (Fiore, et al., 1990). Nearly all state health departments have developed a protocol for investigating cancer cluster reports. The procedures vary greatly, but each mechanism attempts to respond to very real public concern (Warner and Aldrich, 1987; Thacker, 1989).

With the establishment of the Environmental Epidemiology Section in October, 1982, North Carolina began a formal process for evaluating of cancer cluster reports. This effort was enhanced by the re-establishment of a statewide cancer registry in 1988.

Classifying Cluster Reports

Cluster reports are divided into three broad categories: SUSPECTED clusters, REAL clusters and MEANINGFUL clusters.

SUSPECTED CLUSTERS: When a person reports a perceived increased cancer occurrence in a small geographic area, but none is found to exist, then this report is categorized as a "suspected" cluster. These reports are not really clusters at all. The observed cases may appear to represent a cluster partly because cancer is so common (i.e., it strikes one of four people sometime during their lifetime). "Suspected" cluster reports represent about seventy-five percent of all cancer cluster reports received.

REAL CLUSTERS: When significantly more cancers occur than would be expected within a small geographic area and/or in a short time period, then a "REAL" cluster is said to exist. **However,** a REAL cluster is one for which **there is no pattern to the increase** that can suggest an interpretation of potential increased risk. These REAL clusters will occur periodically, simply by chance. For Example:

> In one of every 256 families of four, all four members will have cancer sometime during their lifetime, by chance alone. Assuming a 100-year lifetime, one family of four out of 25,600 families of four could all develop cancer in a single year. That would be a REAL cluster, but it would be due to chance.

REAL cluster reports are often found in communities where there is a large percentage of older persons. Cancer rates increase with age and adjusting for age often explains the observation of higher than expected number of cases. REAL cluster reports represent about twenty percent of all reports received.

MEANINGFUL CLUSTERS: When a cluster is shown to be "REAL" **and** there is **a pattern to the increase** that suggests a group of people at unusually high risk of cancer, then that cluster is classified as "MEANINGFUL." These cluster reports comprise about five percent of all cluster reports received and are the ones that lead to further epidemiologic studies.

BACKGROUND

Historically, the North Carolina cancer cluster evaluation protocol operated from the Environmental Epidemiology Section of the Department of Environment, Health, and Natural Resources. Evaluations of reports of cancer clusters were generally rigorous scientific activities featuring extensive field work, often including interviews and environmental sampling. Some of the routine procedural steps are noted in the discussion of the current protocol (see below). All cluster reports were acknowledged, but usually, only two or three studies were able to be mounted in a single year. This protocol was first used in 1982 when the Environmental Epidemiology Section conducted a cancer cluster study in Cherokee and Macon counties. That study was both time-consuming and incomplete, as only mortality data were available for the statistical analysis of the study population. The findings from the investigation were equivocal.

Following that experience, the Environmental Epidemiology Section joined with representatives from universities and the scientific community to undertake a study of the cancer database needs for

responding to environmental health concerns. With funding from the Office of Technology Assessment, this group investigated the cancer databases in other states and recommended that North Carolina establish a population-based cancer registry (Aldrich, et al., 1989). The registry was funded and is located in the Division of Statistics and Information Services of the Department of Environment, Health, and Natural Resources. When the registry became functional (Fall, 1989), the Environmental Epidemiology Section began negotiations leading to a revised protocol for use in the evaluation of cancer cluster reports (see Figure 1). This protocol was implemented gradually through the Fall of 1989 and became fully operational on January 1, 1990. The experience upon which the present report is based spans the entire sixteen month period from September 1, 1989 to December 31, 1990.

MATERIALS AND METHODS

In North Carolina, suspected cancer clusters may be reported to county health departments, the state health department, a physician, the Central Cancer Registry, or the American Cancer Society. Wherever reports are initially received, they are forwarded to the Cancer Surveillance Section for evaluation. These evaluations consist of ten basic steps *(NOTE: An asterisk indicates the step was also a part of the former protocol).*

Step 1: ***A letter acknowledging receipt of the report.**** The person reporting a possible cancer cluster receives written verification of their report. This letter includes a description of the steps that will be followed in the evaluation and an estimate of the time frame involved. Copies of the letter are sent to the Environmental Epidemiology Section and to the appropriate county health department.

Step 2: ***Verification of reported cases and a search for additional cases.**** A critical step in the cluster evaluation process is identifying all cancer cases in the study area. Relying solely on the respondent's report of cases is not adequate. It is extremely important to verify the accuracy of the diagnosis for the reported cases and to determine if any cases are missing. Prior to 1988 a search for cancer cases through hospital records and local doctors' offices had to be conducted. In a few communities, surveys of residents have been performed to seek additional cases. These instances are usually those involving small communities or communities where a large number of the cancer cases are likely to be still living. After 1987, cancer cases can be ascertained from the Central Cancer Registry for many counties (all North Carolina counties will be completed in the database for 1990 cases and subsequent years).

Step 3: ***Ascertainment of mortality data for the prior twenty years.**** The purpose of this step is to determine what the trends in mortality rates have been in and around the specified area. Some regions of North Carolina have experienced elevated rates for specific cancers for many years; generally these are multiple county areas and represent an objective of research independent of cancer cluster reports. The results of these mortality analyses may influence whether or not a decision is made to proceed with the evaluation of a cluster report, e.g., a cluster report may represent recognition of a regional trend that is already under study.

This is also a point when adjusting for age explains many cluster reports received from areas of the state where there are large numbers of older, retired citizens. Race and sex specific age-adjusted mortality rates for thirty-two cancer sites have been calculated for all 100 counties of North Carolina for 1970 through 1989. Because many cancers are quite rare and many county populations quite small, these rates must be interpreted cautiously.

Step 4: ***Crude estimation of cancer incidence.*** As cancer survival increases, mortality data alone becomes less appropriate in determining whether further evaluation of a cluster report is justified. Thus, the incidence of cancer in communities reporting clusters must often be ascertained. Beginning in 1990, the Central Cancer Registry collects incidence data on all new cancer cases statewide, so that in the future estimates of these rates will no longer be necessary—the actual rates will be available. For studies of reported clusters prior to 1990, an estimate of the expected number of cases is made (using national rates) to determine what the expected number of cancer cases would be; this may then be compared to the number of cancer cases identified in study area (see Step 2).

Step 5: ***Statistical analysis of the incidence and mortality data.*** The computer software CLUSTER was developed in North Carolina with federal funding from the Agency for Toxic Substances and Disease Registry (Aldrich, 1990). This computer program provides twelve different statistical tests for analyzing the patterns of occurrence for rare health events. When the observed number of cancer cases greatly exceeds the number of cases expected, this is one criterion that a cluster exists. Because many cancers are quite rare, an "increase" may sometimes only involve two or three cases; special statistical methods are used for studying these rare events. Similarly, an overall cancer rate may not be elevated (e.g., for a whole county), but one subgroup of the population may be experiencing more cancer cases than they should (e.g., a single neighborhood, black women, etc.), based on the population in the community. Analyses by population subgroup are a part of the CLUSTER capabilities, as well as studies of spatial patterns and time trends among cancer cases.

Step 6: ***Review of the relevant scientific literature.**** As one step for evaluating each cancer cluster report, scientific articles are reviewed. The articles studied are related to the particular cancers that may comprise the reported cluster. Also, scientific articles will be reviewed related to health effects from exposure to an agent or an exposure source that the community may cite as a part of the cluster report. Cancer is comprised of many diverse disease processes and there are many hypotheses for risk factors for virtually all cancers. Identifying known and suspected risk factors of specific cancers can guide the evaluation of a cluster report to exposures which might not otherwise have been suspected. State agency records are accessible during a cluster evaluation for determining the location of specific industries or hazardous waste sites, particularly those from which there are potentially carcinogenic emissions.

If cluster report evaluations are to serve as a means for identifying new environmental risk factors for cancer, a necessary step is to assess the presence of risk factors which may already have been identified from other cluster studies. Similarly, the results of MEANINGFUL cluster reports are published whenever possible so that researchers in other states can be informed of what risk factors may have been identified from North Carolina's cancer cluster reports.

Step 7: ***A site visit is always made to the location reporting a cancer cluster*** (whether citizens are contacted or not). These visits are made in the course of routine travel related to Central Cancer Registry operations, not as trips solely for visiting a cluster community. This approach to site visits is based largely on financial considerations; as such it can lead to some cluster sites being visited sooner than others. On the site visit, a map is prepared of the entire geographic area, highlighting the source locations of potential hazardous exposures. Often, the environmental source identified by the citizen reporting the cluster is not as "remarkable" as another one that they may not even be aware exists.

This is a point in the cluster evaluation where the literature review may play a pivotal role; suggested risk factors mentioned in the literature may be unknown to the citizen. This is also when community education is a consideration; many cancers have recognized lifestyle, age-specific and genetic risk factors and may have little relation to environmental exposures. Such cancers as lung and breast cancer may comprise the majority of cases that the citizen reports in the cluster; yet a few rare cancers may represent more meaningful environmentally-related events. For these reasons, all cluster report sites are visited; most visits are dead ends (hence visits are made at the convenience of staff), but occasionally a previously unsuspected environmental hazard is identified. That is also why it is important that all cluster reports be evaluated; the increased number of cancer cases that offer a clue to environmental cancer risks may not be those that drew the informant's attention to report the cluster.

Step 8: ***On-site meeting with area residents (if requested).**** This is the point at which educational information is provided to residents about their cluster report and about cancer in general. These educational sessions are always coordinated with local health agencies (e.g., county health department, American Cancer Society). This coordination is a effort to promote broader and continuing cancer educational activities for local communities.

Step 9: ***Final report of conclusions and recommendations.**** These reports are provided to all parties associated with the cluster (e.g., county health department); these reports are "public" documents, available to all who request a copy. Some reports are quite detailed, while others are relatively brief, depending on the availability of data and the findings of the evaluation. The information related to personal histories, like all individual records, are confidential.

Step 10: ***Entry into a continuing file of Cluster Reports.*** All communities that report a cluster become a site for continuing surveillance. Based on the statewide database being created through the Central Cancer Registry, the cancer experience for each community will be monitored for a minimum of five years. The specific cancers that comprised the cluster report will be studied, as will other cancers that may have a relation to environmental exposures.

Close attention is paid when a second cancer cluster report is received from the same or a nearby community. The previous cluster file will be reviewed and the maps prepared from earlier site visits are inspected. Occasionally, cluster reports will be evaluated simultaneously from neighboring areas, which can provide a cost savings as well as a more productive process for evaluating disease patterns.

The duration or timing of the steps of the evaluation protocol may vary with the individual cluster report; however, the sequence is always maintained (Figure 1). All cancer cluster report evaluations are monitored through periodic activity reports, of which this report is one. When a cluster evaluation results in inconclusive evidence of clustering, the community represented by the cluster report will be kept under surveillance for a minimum of five years. When an evaluation indicates a potentially MEANINGFUL increase in cancer occurrence, it is referred to the Environmental Epidemiology Section for further investigation. Subsequent investigations usually include detailed case reviews and on-site interviews, and if necessary, environmental sampling and monitoring of relevant residential exposures. In some instances, a grant proposal may be prepared to seek federal funds to facilitate further study of the reported cluster.

RESULTS

Between September 1989 and December 1990, fifty-two disease cluster reports have been received from thirty-one counties throughout North Carolina. Forty-nine of these reports related to cancer (Table 1) and three involved other health events (Table 2). In addition, four re-evaluations of cluster studies from prior years were conducted.

Of the forty-nine cancer cluster reports, the Cancer Surveillance Section evaluated forty-three and six reports were managed by others — one by the Environmental Epidemiology Section; one by a local physician from Washington County who reported a potential cluster of colon cancer cases; two by the epidemiologist in the Guilford County Health Department; one by a University of North Carolina researcher (Dr. Carl Shy); and the final one by a graduate student from the Bowman-Gray School of Medicine. Twenty-seven of these cluster reports have been closed, eleven are still in active study and another eleven are awaiting the start of active evaluation ("Pending"). Of the closed reports, five were determined to be REAL clusters of which three were deemed to be MEANINGFUL. Each of these five cluster evaluations are described below:

Brain Cancer in Rowan County — *This report was submitted by a local physician who believed he had seen an increase in the brain cancer cases in his medical practice. Following this report, the Environmental Epidemiology Section reviewed 260 medical histories (in seven hospitals) over the next year which represented all new brain cancer cases for Rowan County and its neighboring counties from 1980 to 1989. The case histories include details of the tumors (dates of diagnosis, cell types) and any known risk patterns (age, occupation, smoking history, etc.). Several cases initially identified by the informant were excluded from the "cluster" because the cancer of the brain reported to the investigators was spread to the brain from other body sites, or because the person was diagnosed with brain cancer prior to moving to Rowan County.*

Statistical analyses indicated that an unusual pattern of brain cancer incidence had occurred in Rowan County, although not an increased rate of disease (Table 3). For eight of the years of the eighties, very few brain cancer cases occurred in the "cluster area." But in 1985 and 1989, most of the Rowan County brain cancer cases occurred in the "cluster area." For the county as a whole, however, no overall increase in brain cancer occurred. The observed "sudden increase" actually followed periods of low occurrence. This pattern of brain cancer occurrence did not suggest an environmental risk. The study results were presented by written report and through a local press conference.

Brain Tumors in Northampton County — *This report was submitted by the county health director who was concerned about increased occurrence of brain tumors and the possible association with a local industry. A literature review indicated that the relationship to the suspected industry was plausible and had been observed by others (Rabotti, et al., 1966; Morantz, et al., 1985). Community residents assisted health department personnel in identifying living brain tumor cases; the Cancer Surveillance Section performed a parallel search for deceased cases.*

An inspection of the 1984-89 observed-versus-expected case pattern indicated eighteen brain tumors occurred when twelve were expected. The race-sex pattern was not consistent with the national pattern nor with the county's population characteristics. A subset of four cases occurred in proximity to the suspect industry. The possibility that these cases represented the increase could not be dismissed, and as a result, this cluster was referred to the Environmental Epidemiology Section for further study.

Pediatric Cancer in Gaston County — *This cluster report was submitted by the parent of one of three cases of a rare pediatric tumor believed to have occurred in a short period of time in a small municipality in Gaston County. The search for additional cases from 1970 to 1989 indicated that there were two of these rare pediatric cancer cases in the mid-seventies followed by an eleven-year hiatus and then six cases in the next 30 months. These latter cancer cases were the subject of the study. A review of the scarce literature for this tumor revealed that researchers in North Carolina had previously identified the increased rates for this cancer within a twelve-county region (Grufferman, et al., 1982).*

The statistical analysis by the Cancer Surveillance Section indicated that the cases were not randomly distributed. Some of the previously identified risk factors for this cancer were also found with these cases. Since these cases involved children, the distribution of birth defects in Gaston County was also examined using data from the N.C. Birth Defects Registry. No geographic clustering was observed for birth defects. Despite this finding, the presence of several large industries and two recognized hazardous waste sites in proximity to several of the cancer cases led to this cluster being referred to the Environmental Epidemiology Section for further study.

Non-Hodgkin's Lymphoma in Granville County — *A county commissioner referred this potential cancer cluster to the Cancer Surveillance Section. The residents of this small community were quite concerned about an overall increase in cancer, but especially Non-Hodgkin's Lymphoma (NHL). The analyses of the Granville County mortality experience revealed that their rates were not elevated over those of the state. Consequently, further evaluation activities by the state would not be pursued. Upon hearing of these findings however, local residents organized a citizen's task force to extend the data analyses further by collecting cancer incidence data for 1975 to 1989. This well-organized community effort identified over 130 cancer cases, nine of which were non-Hodgkin's lymphomas. The citizen's task force also collected emissions data for a dozen local industries.*

Using the citizen-identified cases, a REAL increase for lymphoma occurrence was found, but there was no particular spatial or temporal pattern for the cases. There was also a visually identifiable aggregate of colon cancer cases, but overall there was no increase in colon cancer occurrence. None of the cancer patterns could be linked to any of the paths of industrial emissions; and only one company was determined to represent a potential hazard. This cluster report was closed with the assurance that surveillance would be maintained for this community. While the work of the citizen's task force did not change the findings regarding cancer clustering, it did provide better data for the analysis and a further opportunity for education to the community about cancer.

Colon Cancer in New Hanover County — *The county health director reported this cluster of four intestinal cancers among neighbors, living in extremely close proximity. Three of the four colon cancer cases were under 65 years of age, an unusual distribution for cancer at this anatomic site. This region of the state has been the focus of much study because of drinking water contamination (e.g., trihalomethane formation). Each of the residents' drinking water was taken from a private well which was suspected to be contaminated with hydrogen sulfide. This cluster report was referred to the Environmental Epidemiology Section for testing of the drinking water supplies. In light of the proximity of another "closed" cluster report to this one, a recommendation was also made that surveillance be maintained for cancer occurrence in both of these communities.*

In addition to the study of cancer clusters, the Cancer Surveillance Section and the Environmental Epidemiology Section perform special studies and apply for federal grants to fund large research efforts in North Carolina. A special study of brain cancer in North Carolina is in progress. The information from both the Rowan and the Northampton clusters figures significantly in the design of that research effort. A federal grant proposal is being prepared to conduct a more thorough study of the several counties potentially involved in the rare pediatric cancer cluster in Gaston County and of the environmental hazards identified through that investigation. Finally, a large study of leukemia patterns in the state is also under way; this is associated with findings from several cluster report evaluations.

FOLLOW-UP OF CLOSED CANCER CLUSTER REPORTS

With the additional capabilities that are now available for the statistical analysis of cancer cluster reports, and because of the continuing interest expressed by three of the communities that had reported earlier cancer cluster reports, three evaluations for cancer clustering were re-analyzed for this report. Also, a search for evidence of leukemia clustering was repeated due to continuing interest by the Environmental Epidemiology Section.

Leukemia in Cherokee County *— Local residents suspected increased cancer occurrence due to the aerial spraying of herbicides in the forests of western North Carolina. Researchers evaluated the pattern of mortality for Cherokee County and seven surrounding counties using statistical tests. No pattern of increased cancer occurrence was found to be associated with any potential environmental hazard. The finding of a generalized increase in all cancers for two counties (Cherokee and Macon) led to a recommendation of further study, with an expanded time period.*

The Cancer Surveillance Section re-analyzed the leukemia data for these eight counties and extended the analyses up to 1988 (Table 4). Macon County had two time periods that showed evidence of temporal clustering, 1979-81 and 1987-88. For Cherokee and Haywood counties as well as the region as a whole, the years 1980-81 also showed increased leukemia mortality. It is intriguing that the cancer occurrence for the years 1980-81 of the previous study was the basis upon which a follow-up analysis was recommended; yet these very years (1980-81) may now be seen to represent the peak of leukemia occurrence for the region. It will be interesting to monitor future cancer patterns for these counties.

Leukemia and Lymphoma in Burke County *— Researchers from the University of North Carolina conducted a "nearest-neighbor" analysis of several cancer cases in Burke County for the period 1970-79. Their results did not indicate clustering for leukemia or lymphomas as reported by citizens. Clustering of lung and prostate cancers was found, however. The CDC also evaluated this leukemia/lymphoma pattern and found no evidence of increased occurrence.*

The Cancer Surveillance Section analyzed the lymphoma incidence data for Burke County for the 1980-89 period. There is still no evidence of increased occurrence, but the ten-year pattern is interesting. Of the fourteen cases in these ten years, eight occurred in 1980-82 (three, three and two cases respectively). Two of the 1980 cases lived close to each other, but none of the others lived particularly close, nor was there any unusual age, race or sex pattern evident. The fact that two cases lived near the location of the earlier suspected cluster is also notable. Further surveillance of the leukemia and lymphoma patterns in Burke County is in order. An evaluation has been completed for lung cancer in Burke County and no increased occurrence was found.

Cancer in Davie County *— A request was submitted to the Environmental Epidemiology Section in 1986 for a study of suspected higher-than-expected cancer rates in Davie County. Residents were particularly concerned about hazardous emissions from industries near the town of Cooleemee. The community organized a survey to identify additional cases; organizational efforts were so successful that a unit of the American Cancer Society was formed from that beginning. However, the conclusion from this study was that there was no evidence of increased cancer rates.*

Using the CLUSTER software, an analysis of the cancer experience in Davie County was re-evaluated and extended through 1988. Over the 1984-88 period, Davie County's liver and bladder cancer death rates were elevated above the state rates; however these excesses were based on very small numbers (i.e., averages of one death or less per year) and therefore are not considered reliable estimates. The Davie County lung, leukemia, kidney and brain cancer death rates were lower than the state's.

Myelogenous Leukemia in North Carolina *— The Environmental Epidemiology Section requested an analysis of 1984-88 age-adjusted mortality rates of myelogenous leukemia. Their objective was a search for potential clusters associated with point sources of airborne emissions of benzene. A visual inspection of a map with the myelogenous leukemia rates was performed at the time of the initial request. Now a statistical analysis for evidence of clustering is available using the CLUSTER software (see Figure 3).*

Twenty-six counties had very high myelogenous leukemia mortality rates ($\geq$ 3.4/100,000); some of these rates in extreme eastern and western counties may be unstable due to the very small numbers of cases involved. The state and national rates of myelogenous leukemia mortality were 2.5/100,000. Rates for forty-four counties were significantly higher (i.e., $\geq$ 2.7/ 100,000). The distribution of these counties with significantly elevated rates provides evidence of several clusters that may offer leads for further investigation (probability of observed clusters $p < 0.001$; $p < 0.05$ for counties with very high rates). A special study of leukemia occurrence in the central Piedmont counties is already under way.

DISCUSSION

Many public health experts believe that evaluating cancer cluster reports is a valuable service. The new protocol developed for evaluating cancer cluster reports has greatly increased the responsiveness to citizen concerns, e.g., twenty-seven cluster reports were "closed" using the new protocol in the comparable time that one report (Rowan County) was evaluated using former procedures. The new protocol already provides greater cost-effectiveness and timeliness in handling cancer cluster reports through the use of statistical analyses of the available data in place of the costly process of collecting new data for each cluster. As the new protocol is refined, it will provide a systematic approach to cancer cluster investigation and analysis; this will mean a straightforward, step-by-step process that can be explained to persons reporting clusters.

Also, much greater contact is being made with local residents to provide educational programs (nine on-site lectures were provided as a part of the twenty-seven "closed" cancer cluster evaluations). These community presentations help to assuage community concerns and extend a positive response to public inquiries. These educational programs provide answers to legitimate questions about both cancer prevalence and possible environmental associations. To facilitate these educational goals, an informational brochure was developed in collaboration with the American Cancer Society; it is available by request. In addition to the evaluations described in this report, the staff of the Cancer Surveillance Section have been involved in four consultations related to potential cancer clusters in North Carolina, one in each of Harnett, Robeson, Burke and Catawba counties.

This greater effectiveness and visibility have led to reports of disease clusters other than cancer being referred to the Cancer Surveillance Section. Three such cluster reports are:

A potential cluster of Multiple Sclerosis in Alleghany County.

Two cases of a rare dermatologic condition diagnosed in neighbors in Cabarrus County.

A series of spontaneous abortions, in a two-month period, among neighbors in Wake County.

However, for so many cluster reports, even the time required for site visits and data analyses compels the Cancer Surveillance Section to do cluster evaluations as time permits and where travel makes site visits convenient. The work with cancer clusters will continue, although recent budget constraints will lengthen the time to complete evaluations. The twenty-seven reports described here as "closed" averaged three months for evaluation; this does not include the extensive Rowan study that required 14 months for completion. Such rigorous and detailed efforts must be reserved for those clusters that truly warrant such intensity, including those identified through proactive cancer surveillance.

CONCLUSION

Cancer cluster investigations may represent a social service more than scientific research. Cluster investigations should not be viewed strictly for their scientific research merit, but also for their role as an important interactive public health activity. "The public is increasingly demanding answers regarding possible associations between [cancer] and the environment." (Fiore, et al., 1990). The evolving procedures described in this report address these concerns with a sound epidemiologic approach to responding to cancer cluster reports.

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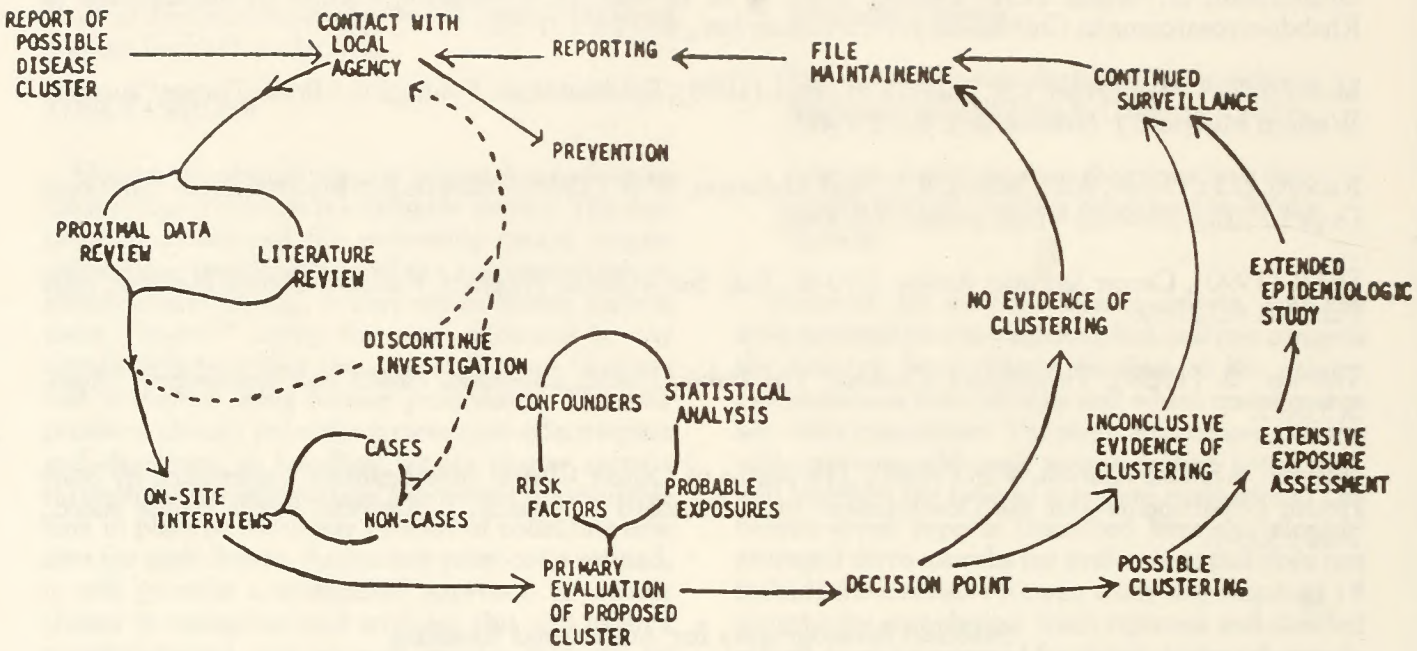
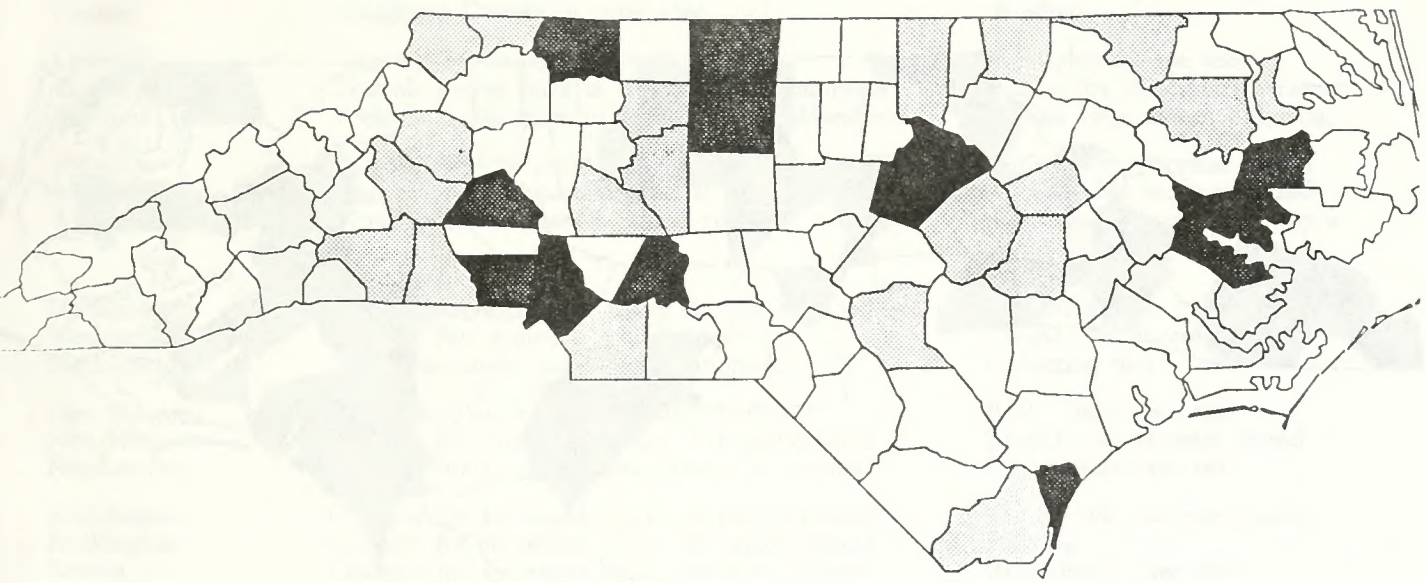


Figure 1 — North Carolina Protocol for Evaluating Cancer Cluster Reports

Cancer Cluster Reports

Received By County

September 1989 Through December 1990



N.C. Cluster Reports

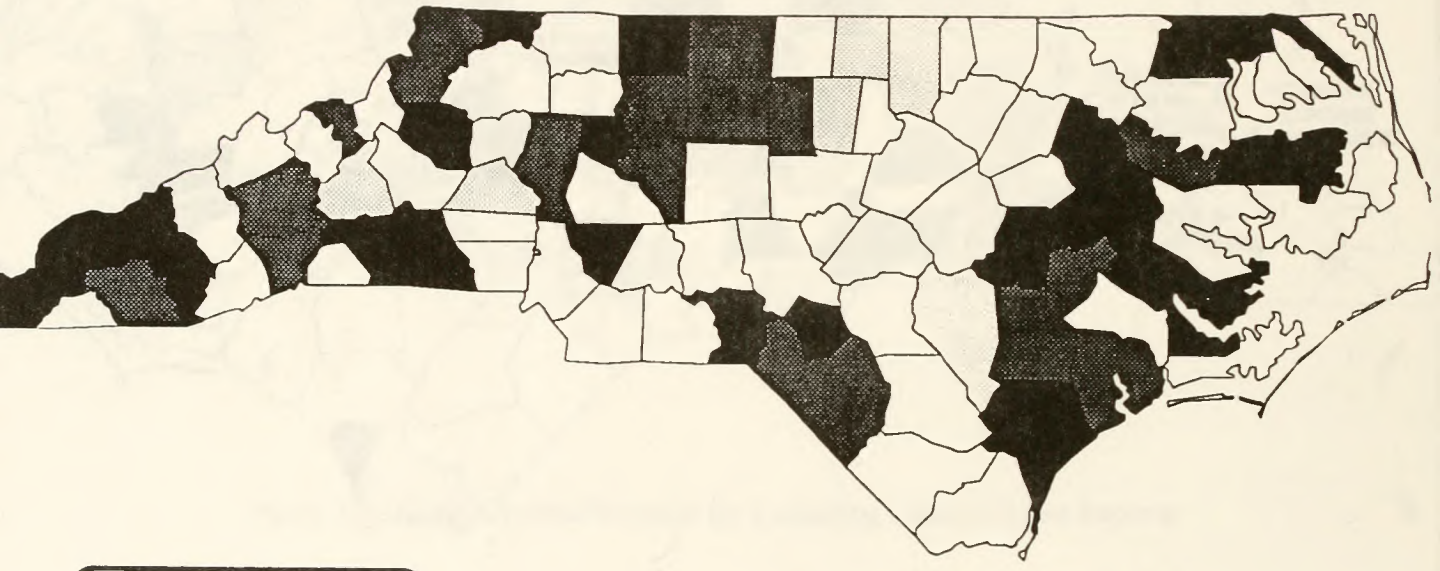
no cluster reports received
1 cluster report received
2-3 cluster reports received
4 or more reports

Figure 2 — Cancer Cluster Reports by County 9/1/89 to 12/31/90

Age- Race- Sex Adjusted Death Rates for Myelogenous Leukemia

North Carolina, 1984-88

(1970 U.S. standard)



Deaths per 100,000 Population

- 0.00 to 2.49
- 2.50 to 2.69
- 2.70 to 3.39
- 3.40 to 8.00

*** Rates of 2.7 or greater were significant at .05 level**

Figure 3 — Map of Myelogenous Leukemia Mortality 1984-1988
Age- Race- Sex-adjusted Rates (1970 U.S. standard)

Table 1 — North Carolina Cancer Cluster Reports Received 9/1/89 to 12/31/90

County	Description	Status
Alleghany	Possible excessive rates in small town	Pending
Ashe	Concern for excess cancer in the county*	Collecting data
Beaufort	Suspected drinking water contamination	UNC—study in progress
Beaufort	Concern for excess cancers in local area	In active evaluation
Bertie	Possible increased cancer among neighbors	Closed—No increase found
Brunswick	Brain cancer around nuclear power plant	Closed—No increase found
Burke	Fear of lung cancer due to plant emissions*	Closed—No increase found
Caldwell	Kidney cancer cases in small area	In active evaluation
Catawba	Concern for cancers near industrial park	Closed—No increase found
Catawba	Six neighborhood cancers in two years	Closed—No increase found
Chowan	Concern for local paper plant emissions	In active evaluation
Cleveland	Multiple cases in one neighborhood*	Pending
Cumberland	Eight cancer cases among 30 homes	Pending
Davidson	Concern for cancers near industrial park	Closed—No increase found
Forsyth	Four gastrointestinal cancers in neighborhood	Closed—No increase found
Gaston	Three rare pediatric tumors in small town*	Real Cluster—see text
Gaston	Concern for cancers near industrial park	Closed—Familial grouping
Gaston	Hodgkin's Disease in rural area	Pending
Granville	Concern for increased lymphomas*	Real cluster—see text
Guilford	Possible excess rates in Summerfield community	Closed by local Health Dept.
Guilford	Possible excess rates in Jamestown neighborhood	Health Department following
Johnston	Concern for increased cancer in neighborhood	Closed—No increase found
Mecklenburg	Concern for increased cancer in neighborhood	Closed—No increase found
Mecklenburg	Three leukemia cases in small area	Closed—Cases occurred over a long time period
Mecklenburg	Concern for increased cancer in neighborhood*	Collecting data
Mecklenburg	Concern for industrial emissions	Closed—No increase found
Mecklenburg	Six breast cancer cases in neighborhood	Collecting data
New Hanover	Four colon cancer cases in neighborhood	Real cluster—see text
New Hanover	Concern for increased cancer in neighborhood	Closed—No increase found
Northampton	Concern for increased brain cancer in county*	Real cluster—see text
Rockingham	Concern for increased cancer in neighborhood*	Closed—No increase found
Rockingham	Concern for increased cancer in neighborhood	Pending
Rowan	Concern for increased brain cancer in county	Real cluster—see text
Rutherford	Concern for increased cancer in neighborhood	Pending
Stanly	Concern for excess cancer in the county*	Collecting data
Stanly	Concern for excess cancer in the county	Collecting data
Surry	Excess upper respiratory cancer suspected	Student project—closed
Surry	Concern for increased cancer in neighborhood	Pending
Surry	Concern for increased cancer in neighborhood	Pending
Union	Concern for increased cancer in work place	Pending
Wake	Concern for increased cancer in neighborhood	Closed—No increase found
Wake	Concern for increased cancer in neighborhood	Closed—No increase found
Wake	Concern for increased cancer in neighborhood	Closed—No increase found
Wake	Concern for increased cancer in neighborhood	Pending
Warren	Concern for cancers in household	Closed—Familial grouping
Washington	Concern for colon cancer excess in community	Local M.D. following
Washington	Concern for local paper plant emissions	In active evaluation
Wayne	Concern for increased cancer in neighborhood	Closed—No increase found
Wilson	Concern for increased cancer in neighborhood	Pending

*Educational program presented.

Table 2 — North Carolina Cluster Reports of Other Health Effects Received 9/1/89 to 12/31/90

County	Description	Status
Alleghany	Multiple Sclerosis—multiple cases	In active evaluation
Cabarrus	Lobular Panniculitis—Two young girls No suspected environmental factors	Searching for additional cases
Wake	Three spontaneous abortions in close friends	In active evaluation

Table 3

Brain Cancer Cases for Rowan County As A Whole, the Cluster Area and the Balance of Rowan County 1980-89; Also the Observed/Expected Ratio for Five-year and Ten-year Intervals[1], Rowan County Compared to the U. S. and to the Six-County Region

Year	Suspected Cluster Area	Balance of Rowan County	All of Rowan County	Rowan County[1] Age-Adjusted Incidence Rate	U.S. O/E Ratio[2]	Six County Region O/E Ratio[3]
1980	0	4	4			
1981	2	2	4			
1982	0	0	0	---> 2.6/100,000	0.42	0.58
1983	1	4	5			
1984	0	2	2			
1985	5	2	7			
1986	0	7	7			
1987	3	3	6	---> 5.5/100,000	0.89	0.90
1988	2	4	6			
1989	5	0	5			
			Ten-year	3.9/100,000	0.64	0.75

[1]Because of the small numbers of cases, it is customary to use an aggregate time period (1980-84 and 1985-89 and 1980-89 in this case) for comparison to national rates and regional rates. This is so that the Observed/Expected Ratio will be most stable. A more thorough report of the statistical analysis is available by request.

[2]The U.S. Rate for the entire 1980 to 1989 time interval was 6.2 per 100,000 population (SEER, 1990); the Observed/Expected ratios are obtained by dividing each of the respective Rowan County rates by the 6.2 rate of the United States.

[3]For Rowan County and its five neighboring counties (the Six-County Region), the respective incidence rates (per 100,000) were 4.5 for 1980-84; 6.1 for 1985-89, and 5.3 for 1980-89. The Observed/Expected ratios are obtained by dividing each of the respective Rowan County rates by the corresponding Six-County Region rate.

Table 4

Leukemia Cases for Western North Carolina Counties, 1976-1988; Also results of the Scan, Negative Binomial and Poisson Tests — using the CLUSTER Software

County	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	Maxima Scan Yrs[1]	Neg Bin/ Poisson[2] p value
Cherokee	2	0	0	2	4	2	1	3	1	1	4	1	2	1979-81	0.52
Clay	0	1	0	0	1	0	0	2	0	0	1	0	2	none	0.07
Graham	1	0	1	0	0	0	1	1	0	1	0	2	1	1987-88	0.39
Macon	1	1	0	3	8	1	2	2	3	0	2	4	8	1979-81 1987-88	0.03
Swain	0	1	1	2	1	2	2	1	0	0	3	3	0	1986-87	0.19
Jackson	0	1	1	1	1	1	3	0	2	2	3	3	0	1986-87	0.27
Transylvania	3	0	0	1	1	1	3	1	5	0	1	3	1	1982-84	0.72
Haywood	3	5	4	3	5	8	4	3	2	5	3	2	3	1980-82	0.62
TOTAL AREA	10	9	7	12	21	15	16	13	13	9	17	18	17	1980-82	0.22

[1]Within each of the counties, there was a period of "highest" occurrence; this maxima is what the Scan statistic searches for. An inspection of when these periods of high occurrence "line up" may reveal a pattern of disease occurrence in time. Macon, Cherokee and Haywood counties and the entire region share a high temporal grouping for the years 1980 and 81—the focal time period for the earlier "cluster" report.

[2]Negative Binomial probabilities were used wherever appropriate (Cherokee, Clay, Macon and Transylvania counties and the total area); otherwise Poisson probabilities were used (Graham, Swain, Jackson and Haywood counties). These p-values represent the probability of the observed case occurrence over the 13-year run being the result of chance. For Swain and Jackson counties a 12-year run was utilized as those counties had zero cases in 1988.

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